-2-



consider das a Petitien for Extension of Time under 37 C.F.R. § 1.136(a), with authorization to deduct the applicable fee (large entity) under 37 C.F.R. § 1.17(a) from our Deposit Account No. 02-2553.

IN THE SPECIFICATION

In accordance with 37 C.F.R. §1.121(b)(i) and (ii), please amend the specification as indicated below.

Replace the paragraph bridging pages 8 and 9 with the following:

In a more particular aspect, the invention includes a DNA molecule of one of the indicated sequences in which the DNA molecule includes the sequence TGAACTNNNNNTGAACT, where "N" can be any nucleotide and there can be 0 to 5 N (SEQ ID NO:39), wherein x has a value of up to 5. This sequence is conserved in all three of the nucleotide sequences identified as having promoter activity, particularly where x is 5. Even more particularly, the invention includes such a DNA molecule in which the sequence TCTGASSAAGKTAAC (SEQ ID NO:40) occurs downstream from the sequence TGAACTNNNNNTGAACT, where "N" can be any nucleotide and there can be 0 to 5 N (SEQ ID NO:39). Even more particularly, the sequence includes the sequence AATT between the sequence TGAACTNNNNNTGAACT, where "N" can be any nucleotide and there can be 0 to 5 N (SEQ ID NO:39) and the sequence TCTGASSAAGKTAAC (SEQ ID NO:40), the AATT having been found immediately downstream of the sequence TGAACTNNNNNTGAACT, where "N" can be any nucleotide and there can be 0 to 5 N (SEQ ID NO:39). It has been observed that there can be up to six nucleotides between the sequence TGAACTNNNNNTGAACT, where "N" can be any nucleotide and there can be 0 to 5 N (SEQ ID NO:39) and the sequence TCTGASSAAGKTAAC (SEQ ID NO:40). There can also be the sequence CAATTAAAGA (SEQ ID NO:41) upstream of the sequence TGAACTNNNNNTGAACT, where "N" can be any nucleotide and there can be 0 to 5 N (SEQ ID NO:39). In a particular aspect, the nucleotide sequence having promoter activity includes the sequence CAATTAAAGATGAACTTTGGGTGAACTAATT (SEQ ID NO:42) and the sequence TATAA. Particularly, the sequence TATAA is downstream of the sequence TGAACTNNNNNTGAACT, where "N" can be any nucleotide and there can be 0 to 5 N (SEQ ID NO:39), and more particularly, the sequence TATAA is downstream of the





sequence TCTGASSAAGKTAAC (SEQ ID NO:40) and it can be spaced up to about 55 nucleotides downstream from the sequence TGAACTNNNNNTGAACT, where "N" can be any nucleotide and there can be 0 to 5 N (SEQ ID NO:39).

Replace the last complete paragraph (lines 32 to 34) on page 12 with the following:

 C^2

Figure 15 shows promoter sequences of human, mouse and zebrafish P450RAI (SEQ ID NOs:33, 34, and 35, respectively). The boxed regions show highly conserved regions while the arrows indicate spaced apart consensus sequences of RAREs.

Replace the first paragraph on page 15 with the following:

 \sim 3

In order to facilitate cloning of the PCR products, several changes were made to the reactions. Primers which included Eagl restriction endonuclease sites were used in the reamplification. Based on results obtained in the differential display analysis, the upstream 5'-TGCCAGTGGA-3' (SEQ ID NO:26) primer was replaced by 5'-GTAGCGGCCGCTGCCAGTGGA-3' (SEQ ID NO: 29) and the downstream poly-T primer, 5'-TTT TTT TTT AG-3' (SEQ ID NO:6), was replaced by 5'-GTAGCGGCCGCT₁₂-3' (SEQ ID NO:30). In addition, the reaction volume was increased to 40 µl, isotope was omitted and 20 as opposed to 40 cycles were performed. 5 µl aliquots of the PCR reactions were removed and the products were visualized by electrophoresis in a 1% agarose gel followed by ethidium bromide staining and UV illumination.

Replace the first paragraph on page 24 with the following:

CH

Cloning of Zebrafish P450RAI promoter. An adult zebrafish genomic library (1.0 x 10⁶ pfu) was screened with the full length cDNA corresponding to zP450RAI and positive plaques purified through secondary and tertiary screening. Lambda DNA corresponding to positive plaques was prepared, and the inserts from these clones were excised by restriction enzyme digestion with NotI and subcloned into the plasmid SK+ (Stratagene). Genomic clones were analyzed by restriction enzyme digestion using enzymes from the polylinker of SK+, followed by Southern blotting using an oligonucl otide (5'-GTAGCACGGATGGTG-3' (SEQ ID NO:43)) which hybridizes to the